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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/768,932	01/30/2004	David J. Glass	REG 990A	9274

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EXAMINER	
HORNING, MICHELLE S	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 11/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/768,932	GLASS ET AL.	
	Examiner	Art Unit	
	Michelle Horning	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,7,9,11,12,15-20,23 and 27-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *,2,5,7,9,11,12,15-20,23 and 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is responsive to communication filed 9/11/2006. The status of the claims is as follows: claims 3-4, 6, 8, 10, 13-14, 21-22, 24-26 and 30-31 are cancelled and claims 1-2, 5, 7, 9, 11-12, 15-20, 23 and 27-29 are under current examination.

Applicant's election of Invention I in the reply filed on 9/11/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Election of SEQ ID NO:2 is acknowledged. SEQ ID NO:2 has been searched and is free of the prior art. The claims under current examination, however, are not limiting to SEQ ID NO:2.

Claim Rejections

35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 12 recites a "human FcΔ1" yet this is not disclosed in the specification. "Fc(ΔC1)" is recited in the specification on page 7. Appropiate correction or further clarification is required.

35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 5, 9, 11, 15, 17, 19-20 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Kruskal et al (1992). The limitations of the above claims are as follows: 1) a nucleic acid encoding a fusion polypeptide comprising one or more domains of a CCR or a fragment thereof, one or more domains of a CR or a fragment thereof and a FC; 2) wherein the CCR is selected from human CCR5 or a fragment thereof, human CXCR4 or a fragment thereof and a lectin-binding receptor; 3) wherein the CR is selected from a human CD4 or a fragment thereof and a lectin-binding receptor; 4) wherein the FC is an immunoglobulin-derived domain, more specifically, selected from the Fc domain of IgG or the heavy chain of IgG; 5) the fusion polypeptide encoded by nucleic acid of limitation #1 above; 6) a method of producing a fusion protein comprising transfection of host cell with nucleic acid for expression and recovery; 7) a fusion polypeptide comprising one or more domains of a CCR or a fragment thereof, one or more domains of a CR or a fragment thereof and a FC; 8) wherein the CCR is selected from human CCR5 or a fragment thereof, human CXCR4 or a fragment thereof and a lectin-binding receptor and 9) wherein the CR is selected from a human CD4 or a fragment thereof and a lectin-binding receptor.

Krustal et al disclose a method of transfecting Cos7 cells with nucleic acid that encode a chimeric receptor containing the ligand-binding ectodomain of the Fc receptor and the transmembrane and cytoplasmic domains of the mannose receptor (see Abstract and Materials and Methods). This chimera led to the efficient ingestion of erythrocytes (Abstract or whole document); thus, according to the definition of FC disclosed in the instant specification, this limitation is met. Further, Krustal et al teach a chimera that comprises a "fragment" of all the domains within the claims. Of note, the specification does not define a fragment and it is taken to mean here as little as a single amino acid. Given that all of the limitations above are met, these claims are rejected.

Claims 1-2, 5, 7, 15, 17, 19-20 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Aullo et al (1992). The limitations of the above claims are as follows: 1) a nucleic acid encoding a fusion polypeptide comprising one or more domains of a CCR or a fragment thereof, one or more domains of a CR or a fragment thereof and a FC; 2) wherein the CCR is selected from human CCR5 or a fragment thereof, human CXCR4 or a fragment thereof and a lectin-binding receptor; 3) wherein the CR is selected from a human CD4 or a fragment thereof and a lectin-binding receptor; 4) wherein the nucleic acid comprises the human CD4 Ig-like domain 1 or a fragment thereof capable of binding gp120; 5) the fusion polypeptide encoded by nucleic acid of limitation #1 above; 6) a method of producing a fusion protein comprising transfection of host cell with nucleic acid for expression and recovery; 7) a fusion polypeptide comprising one or more domains of a CCR or a fragment thereof, one or more domains of a CR or a fragment thereof and a FC; 8) wherein the CCR is selected

from human CCR5 or a fragment thereof, human CXCR4 or a fragment thereof and a lectin-binding receptor; and, 9) wherein the CR is selected from a human CD4 or a fragment thereof and a lectin-binding receptor.

Aullo et al disclose a method of expressing and purifying a protein using *E. coli* (see Materials and Methods). This fusion protein comprises a "portion of human CD4, a membrane protein, which recognizes the HIV glycoprotein gp120" (see introduction). The fusion protein further comprises the N-terminal 389 amino acids of diphtheria toxin in addition to the 178 amino acids of human CD4 that contains the V1 and V2 domains that are sufficient to bind to HIV glycoprotein gp120 (see introduction). Aullo et al teach a chimera that comprises a "fragment" of all the domains within the claims. Of note, the specification does not define a fragment and it is taken to mean here as a single amino acid. Given that all of the limitations above are met, these claims are rejected.

Claims 28-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Nagashima et al (2001). The limitations of the above claims are: 1) an HIV-specific protein capable of binding an HIV viral particle and/or blocking the ability of an HIV viral particle to infect a cell comprising two of the fusion proteins selected from CCR or fragment thereof, CR or fragment thereof, or FC and 2) a composition comprising the above HIV-specific fusion protein and a pharmaceutically acceptable carrier.

Nagashima et al disclose the use of two separate fusion proteins that specifically block HIV entry via blocking virus-cell and cell-cell mechanisms (see whole document). PRO 542 is a tertravalent CD4-immunoglobulin fusion protein that blocks HIV-1 isolates (see Introduction). Further, this prior art reference discloses that the fusion proteins

were formulated in PBS and that HeLa-CD3+ CC-chemokine receptor 5 (CCR5) cells were used for the fusion assay (see Material and Methods). Thus, the claims above are rejected.

35 U.S.C. 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 18 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krustal et al and Aullo et al, and further in view of Wu et al (2000). While Krustal et al and Aullo et al disclose fusion polypeptides comprising fragments as claimed (see above), these references do not teach multimerization of a peptide. Wu et al disclose both the formulation and mechanism of a multimerization of peptide (see

whole document). It would have been obvious to one of ordinary skill in the art to modify the methods taught by Krustal et al and Aullo et al in order to form a multimerized polypeptide. One would have been motivated to do so in order to more efficiently dry the polypeptide product and to increase storage time (see page 14). There would have been a reasonable expectation of success given that such methods are well described in the art. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Krustal et al and Aullo et al, and further in view of Tamma et al (1991). While Krustal et al and Aullo et al disclose fusion polypeptides comprising fragments as claimed (see above), these references do not teach the use of the CΔ1. Tamma et al teach that IgD receptors react with CΔ1 domains via crosslinking experiments (see Discussion). It would have been obvious to one of ordinary skill in the art to modify the teachings of Krustal et al and Aullo et al and incorporate the CΔ1 domain as taught by Tamma et al. One would have been motivated to do so to selectively target cells which bind this domain, such as T cells as shown by Tamma et al (see Discussion). There would have been a reasonable expectation of success given that the underlying techniques are well described in the prior art. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 5, 7, 9, 11, 15, 17, 19, 20, 23 and 27-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Enablement is considered in view of the *Wands* factors (MPEP 2164.01(a)).

Nature of the invention. The claims are drawn to fusion polypeptides and nucleic acids encoding them. The fusion proteins are comprised of CCR, CR and FC.

State of the prior art. At the time the invention was made, many fusion proteins that specifically target HIV entry in isolated cells was known. The prior art further discloses potential target sites and targeting molecules, including lectin receptors or gp120, for blocking HIV infection of cells.

Breadth of the claims. The claims are extremely broad encompassing any and all: 1) CCRs; 2) CR; 3) FC; 4) lectin-binding proteins; 5) HIV isolates; 6) Fc domains of IgG and any and all possible fragments of each. Of note, the claims are not limited to peptide domains of a particular animal, such as human. The fusion polypeptide as claimed can be anything and the domains can be arranged in any order.

Working examples. No working example is disclosed in the specification. All examples are drawn to providing the polypeptides and PCR primers set forth in SEQ ID NOs: 1-18.

Guidance in the specification. The specification provides little guidance regarding how to make or use the invention *as claimed*. The specification provides a lot of theory underlying the actual use of the products as well as how to make and use specific fusion proteins. The effect, however, is not disclosed by the specification and thus, it is not known if the invention would lead to the actual blocking of HIV entry into cells.

Predictability of the art. In the instant application, the Applicants have not disclosed the function of the fusion protein as claimed. Given that the claims are drawn to any and all possible combinations within a fusion protein, there is no way to predict what the effects are of the different proteins.

Amount of experimentation necessary. It would require extensive research to understand the fundamental biology of HIV. Because it is not known what the different possible functions the many fusion proteins will serve, particularly in blocking HIV infection, much experimentation is necessary.

For the reasons above, it would require undue experimentation for one skilled in the art to use the claimed products.

CONCLUSIONS

No claim is allowed. Of note, claim 16 is not limited to SEQ ID NO:2 and thus not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michelle Horning whose telephone number is 571-272-9036. The examiner can normally be reached on Monday-Friday, 8:30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 570-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for unpublished application is available through Private PAIR only. For more information about PAIR system, see htt://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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